developed. None ever did show a rise in temperature, and I have abandoned this idea as a method of demonstrating an undeveloped syphilitic infection.

Summary and conclusions

(1) Penicillin is the most potent remedy now at our disposal for the treatment of gonorrhoea.

(2) With a dosage of 100,000 units and upwards, given in 4 or 5 separate injections over 8–12 hours, a rapid clinical cure of at least 90 per cent of cases of uncomplicated acute or sulphonamide-resistant gonorrhoea can be confidently expected. Of the failures which show a reappearance of gonococci in secretions, a large percentage can be cured by further treatment with penicillin.

(3) Adjuvant treatment is sometimes required for residual urethritis due to secondary infection.

(4) Complicated cases with closed foci of infection do not always react well to penicillin. In such cases foci of infection must be drained before treatment with penicillin is begun.

(5) The best method of treatment of gonorrhoea with penicillin, in the present state of our knowledge, is with doses of not less than 100,000 units given intramuscularly in 4 or 5 separate injections at two-hourly or three-hourly intervals over a period of 8–12 hours. Patients with a gonococcal relapse after penicillin treatment should be re-treated with a higher dosage than that originally used and, if this is unsuccessful, two " courses " of penicillin at 24 hours' interval should be tried.

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DISCUSSION ON THE PRECEDING PAPERS

Brig. T. E. Osmond (the President) thanked Col. Harrison for reading Col. Pillsbury's paper. He said that he had hoped to collect observations on a considerable number of cases ; a large number had been treated, but the patients moved about so quickly that one man's cases today were another man's tomorrow. He had succeeded in getting 148 cases of which 143 were perfectly satisfactory at the end of 6 months, with the possible exception of 4 patients who had refused cerebrospinal fluid examination. There were 3 serological relapses and 2 probable reinfections. If the latter were counted as relapses, the figures would make 3 per cent of relapses, but it had to be remembered that in a certain number of cases relapse had occurred after penicillin therapy before 6 months had passed, so that the actual relapse rate was considerably above 3 per cent.

In one theatre of war, out of 1,471 cases there were 18 infectious relapses or reinfections : 1·2 per cent. The old difficulty of distinction between relapse and reinfection would crop up, and he felt that all recrudescences should be regarded as relapses unless it was certain that they were reinfections. Reinfections would occur if penicillin were the curative agent that it was

thought to be. Of 106 sero-negative cases, 5 showed doubtful or positive serological reactions at the end of 6 months ; of 47 sero-positive cases 13 were positive or doubtful at the same period, and 6 out of 15 secondary cases gave similar results ; this made a total of 24 out of 168, which was not a very satisfactory outcome. There was no doubt that results in Great Britain were not as good as those of Col. Pillsbury.

If the speaker had syphilis himself, and if it were sero-negative, he would have penicillin treatment, but if it were in the sero-positive or secondary stage he would have both arsenic and bismuth treatment, stressing the bismuth. He would suggest a couple of injections of arsenic and one or two of bismuth during the penicillin course and then more bismuth to follow.

Maj. **S. M. Laird** said that he had seen relapses but that he felt rather diffident about talking about them because, as had been mentioned, it was not easy to distinguish with confidence between reinfection and relapse. He had noticed in Table 3 that a rather large number of cases showed the appearance of a sore outside the site of the original chancre ; that might be interpreted as evidence in favour of reinfection. The site of the lesion seemed to be a rather important point in answering the question whether it was a case of relapse or of reinfection. He had seen 8 cases of clinical relapse in a total number of 300 patients treated with penicillin alone with the same routine as that used by the Americans. The follow-up was very inadequate but most relapses had occurred about the fourth month. He found that, during the serological surveillance, the quantitative Kahn test at 2 and 4 months had not thrown any light on approaching relapses, which was rather disappointing. With regard to the cerebrospinal fluid examination at the sixth month, the numbers made were very inadequate ; he felt that to confine one's assessment of the position purely to the position at 6 months would give an unduly favourable view of the results of penicillin treatment, because it would cut out the earlier relapses which were actually seen.

Dr. **A. E. W. McLachlan** said that his experience was comparatively small but was fairly wide. He had observed in the majority of the cases a rapid disappearance of clinical signs, for example, a large gumma of the sternum disappearing completely in 5 days ; on the other hand, he had noticed—rather more often than he liked—the primary sore persisting for some time after completion of 7½ days' penicillin treatment. He wondered whether or not the variations in the results were due to the standard of purity of the penicillin. Certain batches had caused a great deal of local pain on injection and their use had been followed by varying degrees of erythematous rash. In one patient generalized eczema developed and it began to clear up as soon as the penicillin was stopped.

He had noticed, in general, that, in carrying out quantitative blood Wassermann reactions, a fall in titre had paralleled the clinical improvement.

There had been one other observation. In women treated with penicillin for syphilis or gonorrhoea, there was often an alteration in menstrual rhythm. The menstrual periods might be brought on up to a week early by the injection of penicillin, the first period being very heavy, with passage of blood clot, and preceded by severe abdominal pain. The menstrual period after penicillin therapy might be heavy or might be normal ; the third, in all cases, was quite normal. Had other clinicians observed this same sequence ? Were these menstrual sequelae due to the action of penicillin itself, or to the various impurities inseparable from its preparation, which might be absent in the future ?

Dr. **W. N. Mascall** confirmed Dr. McLachlan's observations with regard to menstruation. Almost all his patients had complained of premenstrual pain or uterine pain. Menorrhagia had been a marked symptom and, if the period was nearly due, its onset was expedited. Various brands of penicillin had been used and it did not seem to make any difference which of them was employed. In two cases of early pregnancy there had been actual abortion. He had reached the same conclusion : namely, that it was due not to the penicillin but to some impurities incorporated in the course of its production.

Maj. **Jacobson** said that in his experience in Ceylon with the average under-nourished and slender type of Indian native, especially members of Labour Corps, the pain produced by the injections, which had to be carried on for 7½ days, gave rise to difficulties which were sometimes not easy to overcome. Furthermore, in some cases he was amazed to see that after the end of the penicillin course of 7½ days the chancres had not completely healed, and that even secondary lesions were not as completely removed as they were seen to be under the old treatment. On the other hand, he remembered a case of tertiary syphilis in which all specific and nonspecific treatments had been tried without success, but in which a course of penicillin injections combined with local penicillin application was effective.

In the Far East there were several technical difficulties in applying the penicillin treatment. It was not so easy to guarantee that the staff of native orderlies always followed instructions, and it was necessary to keep a careful watch to see that no blunder was made in the timing of the injections. If penicillin was not given at the correct times, it was not surprising if the results were not so good as might be expected. One had also to take into account the fact that the tropical climate affected the activity of penicillin much more rapidly and much more often than in Great Britain. He hoped that in the future preparations of penicillin would be so improved that these difficulties of treatment might be overcome.

Maj. **Betty Walker** also confirmed Dr. McLachlan's remarks about menstruation. This

increased menstruation occurred in patients who had previously had a normal menstrual cycle. On the other hand, some patients who had had abnormal periods found that after penicillin treatment their periods had become normal.

Dr. F. R. **Selbie,** referring to Col. Pillsbury's paper, asked whether he might show a few slides of the results of experiments in progress at the Bland-Sutton Institute of Pathology, Middlesex Hospital, on the treatment of *Treponema pallidum* infection in the rabbit with penicillin and neoarsphenamine.

In the assessment of the value of drugs in rabbit syphilis one first determined the minimal effective dose, that is to say, the smallest dose necessary to cause complete disappearance of motile spirochaetes from the lesion within 24 hours. This dose of neoarsphenamine was about 10 milligrams (or of mapharside or of Halarsol) (*3-amino-4-hydroxyphenyl-dichlorarsine hydrochloride*), 1 to 2 milligrams per kilogram of body weight. The minimal effective dose of penicillin, divided into 3 equal 3-hourly doses to counteract the effect of rapid excretion, was about 4,500 units per kilogram, or about 3 milligrams of pure penicillin, so that in this respect its effect was about the same as that of an arsenical drug, weight for weight. When neoarsphenamine and penicillin were administered simultaneously the same effect was obtained with one-quarter of the dose of neoarsphenamine and about one-half of the dose of penicillin. There was therefore a synergic action of neoarsphenamine and penicillin in the treatment of rabbit syphilis.

In the long-term assessment of drug action, that is to say, finding the smallest dose necessary to effect cure of the lesion without relapse, results were more irregular, owing to the different degrees of immunity developed by the rabbits. The minimal effective dose, 10 milligrams of neoarsphenamine per kilogram, was usually sufficient to cure the lesions in 70 per cent of rabbits treated, but in a recent experiment it cured only 25 per cent. Failures were obtained with penicillin in doses up to 30,000 units per kilogram, that is to say, 7 times the minimal effective dose, although the immediate effects were as good as those with neoarsphenamine. The results indicated that at least 10,000,000 units of penicillin would be required to ensure a large proportion of cures in man (Selbie and Simon). This, of course, might be too high an estimate, because rabbit syphilis might be more difficult to treat than was human syphilis.

When penicillin and neoarsphenamine treatments were combined, the dose of neoarsphenamine being cut down to 2·5 milligrams and penicillin given in doses of 4,500–30,000 units per kilogram, cures were obtained in all 4 rabbits in one experiment but in only one of 4 in a second experiment, probably because the rabbits were treated at an earlier stage of the infection. In any case it was obvious that the optimal doses for combined penicillin and neoarsphenamine treatment were not yet determined.

It could be said that penicillin was highly effective against syphilis, particularly in its rapid immediate effect which was comparable to that of arsenical treatment ; but it was also apparent that a relatively much larger dose of penicillin would be required to produce a permanently curative effect. Penicillin would be a useful adjuvant to arsenical therapy, but it would be advisable in clinical practice not to reduce the dose of the arsenical drug too much when combining arsenical and penicillin therapy.

Surg. Lt. Cr. **Donaldson** said that they had heard about the results of treatment of syphilis with penicillin by a method requiring in-patient treatment ; it might interest the meeting to know the kind of results obtained in the Navy by the treatment of out-patients. The patients were graded according to the result of the Wassermann test and the treatment consisted of a standard dose of 300,000 units given once in 24 hours for 8 days. The series of cases reported on some months ago by Surg. Capt. Lloyd Jones (Jones and Maitland), had now been followed up, some of them up to 9 months, all of them for more than 4 months. To date in 47 patients who had received daily intravenous injections there was a total of 10 relapses, mainly in the later primary or secondary cases. Since then the same dose had been used intramuscularly. A total of 67 patients had been treated and followed up for a period of 8 weeks, and 2 relapses had been found : one in an early primary case which was sero-negative throughout treatment and one in a middle primary case showing a temporary positive phase after treatment had been commenced.

Pain on injection and various other discomforts experienced by the patients were, he thought, due to impurities in the penicillin ; so much so that it could be predicted, by looking at the colour of the penicillin, which batches were liable to give trouble.

Lt.-col. **A. J. King** said that there seemed to be a tendency amongst certain speakers to decry the value of penicillin in the treatment of syphilis and, while it was well to be cautious, this attitude might be taken too far on too little evidence. A careful survey had been given by Col. Pillsbury, the standard of whose judgment was well known ; but some speakers were putting up against this survey the results of slender experience in order to try to counter the effects on the minds of listeners of the good results which he reported. Col. King had not seen anything like the number of cases which Col. Pillsbury had reported, but he had seen remarkably few relapses in patients adequately treated—treated, that is, according to ideas which were generally accepted at the moment. Because the treatment lasted for so short a time, these relapses were apt to appear more striking than the relapses which used to be seen in the days of long-term treatment with arsenic and bismuth.

Penicillin had an advantage in relation to arsenical treatment, in that with the latter the individual dose kept its potency unless it was grossly misused, whereas minor mistakes in technique of preparation might render penicillin ineffective. He would suggest to those who had described such a high proportion of relapses that they should look again to their technique of penicillin

administration, and also should see a larger number of cases, before they made sweeping statements.

Maj. **J. Marshall** said that his results in cases of early syphilis treated with penicillin alone had not been comparable with those described in Col. Pillsbury's paper. In fact, after 6 months' experience, the results had been so disappointing that he had consulted the literature and discussed the question with Dr. Selbie, in order to try to formulate some more satisfactory method of treating syphilis rapidly and safely. The percentage of failures in his cases appeared to be between 10 and 20. He understood that the present-day view in the United States of America was that the relapse rate after treatment with 2,400,000 units of penicillin was not statistically significantly different from that after treatment with 1,200,000 units ; his own experience bore this out.

In order to reduce the relapse rate he had decided to give a combination of rapid arsenotherapy with penicillin. Previous experience had shown that rapid arsenotherapy with arsenoxide, at the rate of 2 injections in each 3-day period until the required total dosage had been reached, was a safe method. He had therefore given 14 injections of Neohalarsine (arsphenoxide tartrate), 0·09 gramme or mapharside 0·06 gramme over 20 days, beginning the course at the same time as a 7½-day course of penicillin (2,400,000 units). The quantity of arsenoxide given was the smallest amount likely to be of therapeutic value, and at the same time was unlikely to produce grave toxic effects. At the time of speaking no relapse had recurred in the 70 cases so treated and followed up for 3 months or more. A disadvantage of this method was that 20 days' in-patient treatment in hospital was necessary, and he was now trying out a treatment in which daily injections of arsenoxide were given for 10 days, as well as penicillin at the previous dosage level. The patients could be discharged from hospital on the tenth day if all lesions were healed. So far the number of toxic reactions had been quite small. Only 3 patients had had toxicodermal reactions at about the ninth day, by which time they had had nearly the total dosage of arsenic.

Lt.-col. **D. J. Campbell,** speaking of his experience in a theatre of war in which penicillin therapy for early syphilis had been a great boon, said that he thought that he could concur with Col. King when he said that they had been singularly optimistic as regards results. He would admit that impressions were dangerous things, but when one had as enthusiastic a group of workers as he had had—and he was able to keep in touch with them closely during the campaign—he did not think they could all be wrong ! On the matter of the lesions healing more quickly than with other methods, that was not entirely the case. He worked in a theatre in which there was singularly little chancroid and the lesions were reasonably clean, but they did not heal in 7½ days in more than a very small percentage of cases; the average was 10–14 days. Men often reported back with an ulcer which he was sure was due to trauma at the site of the recent chancre, which occurred very early after they got back into battle dress. These cases, when examined by the dark-ground method, were almost always negative. There had not been any serious relapses.

With regard to reactions, all the cases had gone to full treatment without any gross upset ; the usual urticaria was manifest, but in one instance only was there considerable trouble ; in that case every joint became swollen and tender. This occurred on the sixth day of penicillin therapy which, however, was carried on to the full 7½ days with the help of ephedrine ; the man recovered quite satisfactorily.

The matter of relapse would always be a very controversial point and called for very careful consideration. Apart from syphilis, he was perturbed at one stage about the varying results from penicillin treatment in gonorrhoea. There were certain clinics which had a 20 per cent failure rate. They were receiving the same kind of penicillin and using the same technique, and the patients were being infected by intercourse with women from the same areas : Brussels, Ghent, Antwerp and so on. He went into the matter carefully, in case there were any localized source of infection. He was quite satisfied from personal experience that the technique of some clinics was worse than in others ; unless a high standard of technique were attained some relapses might be due to the treatment, apart from anything else. There was no doubt that the early syphilitic patient was cured quickly with penicillin and was liable to reinfection very rapidly and, in a theatre of war such as Col. Pillsbury described, the possibility of reinfection was very important. The assessment of relapses, especially serological relapse, was somewhat difficult, as the patients were moving about from one clinic to another. The difficulty was particularly great when the quantitative Kahn test was used as the measure. Very rarely did two laboratories carry out a parallel course in this test.

Lt.-col. Campbell had had 296 cases which had been adequately followed up. They fell into almost equal parts, in that 149 were sero-negative and 147 were sero-positive. Of the sero-negative cases, 143 out of 149 remained so at the end of 6 months, although a great many of them actually showed a rise to a definite positiveness during the time of treatment. Six cases became positive and remained so ; all of them showed less than 10 Kahn units at the end of 6 months. Their cerebrospinal fluid tests were interesting, in that they showed hardly any deviation from the normal. Of the sero-positive cases 140 became sero-negative and remained so at 6 months ; 6 remained sero-positive. In other words, in both groups the comparative failure was 4 per cent.

Dr. **J. A. Burgess** said that he had had difficulty in persuading civilians to go into hospital for a week's penicillin treatment of early syphilis. He had adopted a scheme, very similar to that mentioned by the previous speaker, of giving 300,000 units of penicillin daily by intramuscular injection for 10 days, combined with a 3 months' course of neoarsphenamine and bismuth. He did not propose to make any remarks about the results, because the cases that he had treated

had been under observation for only a short period. One or two patients had complained of pain but this had not occurred in the majority of cases. The 300,000 units dose had been given to women and none of them had complained of menorrhagia. Samples of blood taken 24 hours after a single injection of 300,000 units of penicillin had shown by examination anything from one-tenth to one-twentieth of a unit of penicillin per cubic centimetre of serum.

Sqn. ldr. **Moynihan** supported Col. King's remarks. He viewed with considerable apprehension the giving of small doses of arsenic without giving penicillin a fair trial. He had had only a small amount of experience but so far he had seen only 2 relapses, one of which might have been a case of reinfection.

With regard to the adequate amount of penicillin, 2,400,000 units had been accepted as the curative dose, whereas it was merely the convenient dose ; there was no evidence that it was the optimum dose. It was only by persevering with penicillin (and altering the dose according to the stage of the disease) that it would eventually be found out whether penicillin was a useful substance by itself or whether the addition of arsenic was required.

It was apparent from Col. Pillsbury's results that early primary syphilis was cured by 2,400,000 units given 3-hourly in 40,000 units. The results with sero-positive syphilis were not so good, but that was the case whatever treatment was given. Instead of employing these small doses of arsenic the penicillin should be continued and a longer or a repeated course given.

Dr. **D. Nabarro** said that from the short-term view it seemed that penicillin was a very valuable remedy, but no one had mentioned the long-term view. Were these patients really going to be cured ? This would be manifested only by the passage of time. Hitherto it had always been thought that syphilis was almost invariably a life-long disease. Would it remain so or were they going to change things by killing the spirochaete quite early ? If this were done the patient was left in a condition in which he might easily be reinfected. His tissues had not had time to respond to the spirochaete and very little immunity reaction had been produced. These patients should be followed up to see whether syphilitic aortic disease, general paralysis and so on developed. Were these going to be the sequelae of the disease treated by penicillin ? Personally he did not know, but he hoped that he might live long enough to see the outcome in patients who had been treated with penicillin. People must beware of over-optimism, for it would be remembered that, when "606" was discovered and found to be a specific for the treatment of syphilis, Ehrlich believed and hoped that the disease would be curable by a single injection—*therapia sterilisans magna*. Unfortunately his hopes were doomed to disappointment ; eventually at least 2 years' treatment proved to be necessary and in some cases an even longer time was required for the eradication of the disease. The same might prove to be the case with the modern methods of intensive arsenic and heavy metal therapy and even with penicillin therapy. It would be necessary to wait 10, 20 or even 30 years, maintaining an efficient follow-up of the treated patients—by no means an easy task—before it could be assumed that syphilitic aortitis, tabes dorsalis or general paralysis would not develop in patients treated by these methods.

Col. **L. W. Harrison** said that he thought that some of the differences of opinion on the results of treatment by similar methods might be accounted for by the work of the laboratories to which blood specimens were sent. Such differences could be "ironed out" by the adoption of a standard test to be used in addition to, or instead of, the tests commonly practised by the laboratories in question. A standard test would be useful also for blood specimens from merchant seamen and other migrants. As regards the type of test which should be used as standard—complement fixation or flocculation—he would strongly advocate complement fixation because (a) the mixing of the antigen suspension was more "fool-proof" than it was for a flocculation test, (b) the results were more easily read, and (c) all reagents except red blood cells could be issued from a central laboratory. For the sake of uniformity in gauging results of treatment, he hoped that members would support his suggestion.

Maj. **Laird** wished to add one or two remarks, because, from the way in which the discussion had gone, he seemed to be in the camp of the careless worker. He ventured to disagree with Col. King on this point. The figures which he had given were incomplete, but they were figures and not impressions, and he had taken considerable trouble to get them. He had also seen clinical relapses in patients treated outside his own hospital, and he thought that the experimental work described by Dr. Selbie of the Middlesex Hospital would suggest that Maj. Marshall and he might not be wrong.

For the last two months he had been giving 400 milligrams of mapharside and 1 gramme of bismuth during the 9 days that the soldier spent in hospital receiving his standard course of penicillin. Discussing the whole problem of penicillin therapy about a month ago, Gen. Poole had suggested that a better approach to the treatment of early syphilis with penicillin would be to give 3-hourly doses of 20,000 units and spread the treatment over twice the usual time, making the period 15 days. It seemed to him that, provided that one could get the effective blood level over each period of 3 hours, then results of therapy spread over 15 days must obviously be better than those of treatment confined to 7½ days. Finally, when the suggestion arose for a course of penicillin treatment in which 2,400,000 units were used, he was pessimistic as to the results and he was still of the same opinion.

Lt.-col. **A. J. King** said that Maj. Marshall's experiences and results were very similar to his own except in one or two points. He noted that Maj. Marshall was more successful in the treat-

ment with penicillin of fresh cases than in that of the sulphonamide-resistant cases. This was contrary to his own experience and the experience of others. He would have expected the reverse of Maj. Marshall's experience, because in gonorrhoea remedies used later in the course of the disease were generally more effective than when used earlier.

His own results in the treatment of primary non-specific urethritis were not nearly as good as were those obtained in treating gonorrhoea. On the other hand, although he was not in a position to give figures, he had seen a fair proportion of successes. As far as his work with gonorrhoea was concerned, the numbers were not large at present ; 300 cases were being followed up but at present there were only 100 cases which were known to have passed a test of cure. Five different courses of treatment had been used. It was interesting that results in patients who received hourly injections were notably better than in those whose injections were more widely spaced.

Dr. **Mascall** wondered what constituted penicillin-resistant gonorrhoea. He had recently seen two patients who had received over 1,000,000 units of penicillin and still had gonococci present in smears. He wondered whether they should not be classed as resistant. There must be a limit to how often one could give intramuscular injections and to how long one could go on administering penicillin. Another interesting case was that of a child with vulvovaginitis who had received 500,000 units and still had gonococci present. These cases seemed to point to a resistant strain.

With regard to the use of penicillin in civil practice, he had stopped using it in certain types of case. A large percentage of the male patients at the clinic were Indian seamen and it was found to be "quick cure, quick return". The stage had been reached at which it was a waste of penicillin to give it to them. One man had 6 separate infections within 8 weeks. These patients were now being treated with the sulphonamides and were given penicillin only if they were resistant to the sulphonamide compounds.

Sqn. ldr. **J. Jefferiss** said that his results had been very much the same as Maj. Marshall's, except that he had found that there had been an improvement after increasing the total dosage from 100,000 to 150,000 units. At present he was using a course of 50,000 units 3 times in one day at 4-hourly intervals, and that was as satisfactory a division of the total dose as any which he had used. He did not think that it mattered whether or not the injections were given at very frequent intervals in treating gonorrhoea. He had had many series of cases treated according to different schemes and it seemed that the larger the total dose the better the results. He had had a small series in which 200,000 units had been used (50,000 units, 4 doses, at 3-hourly intervals) and the results were much better than anything else which he had seen ; but he was rather chary of giving 200,000 units as a regular dosage for fear of increasing the risk of masking any incubating syphilis, so he kept the total dose down to 150,000. To give 50,000 units 3 times in one day seemed to be about as satisfactory as any course which he had used in treating about 1,000 cases.

Dr. **Harkness** was much interested in the type of case of gonorrhoea which was completely resistant to penicillin. He had recently seen a case which had been resistant to 2 courses of penicillin and in which cultures of the urethral discharge yielded only colonies of a Gram negative diplobacillus giving a positive oxidase reaction. It was unfortunate that Maj. Marshall had not had the facilities for making cultural examinations. Col. King had stated that he had had some success with penicillin in the treatment of non-gonococcal urethritis. This might be so when the disease was due to susceptible organisms but, in many cases of non-gonococcal urethritis, the organisms grown by the usual methods for culture were not responsible for the infection.

In a recent addresss to the Society, Dr. Harkness had described granular inclusions in the urethral discharge, and also in certain complications of non-gonococcal urethritis, which might have been the granular phase in the development of pleuropneumonia-like organisms. Cultures for pleuropneumonia-like organisms had been positive in some of these cases. Dienes, Dienes and Smith, and Beveridge had cultured pleuropneumonia-like organisms from genital lesions in the male and female. If these organisms were responsible for the disease, one would expect penicillin to be as ineffective in their treatment as Powell and Rice had found it to be in the treatment of arthritis in rats due to pleuropneumonia-like organisms. Maj. Marshall had stated that 1,000,000 units had had no beneficial effects in a case of Reiter's disease, and this had also been the experience of the speaker. Injections of organic gold salts might subsequently be found to be the treatment of choice in such cases.

Lt.-col. **A. J. King** said that he had been interested in the possibility of organisms of the pleuro-pneumonia group causing some of these non-specific infections and Maj. Salaman had done some very interesting work on the subject which would be published shortly. Arising out of this it had occurred to him that in cases of arthritis, especially when the gonococcus could not be demonstrated in the urethral discharge, it might be effective to use injections of gold, in addition to hyperthermy. This combined treatment had been tried in a few cases, but his immediate impression was that these patients did no better than did those treated with hyperthermy alone.

Maj. **Marshall** (in reply) said that in his paper he had not dealt with the matter of cultures. There was a most interesting American article by Lapenta, Weckstein and Sarnoff in which the follow-up of certain cases by culture methods was described. It was found that the results of treatment with 100,000 units had not been very good. When the dosage was 300,000 units there were 97 per cent of cures (established by culture examinations). The

subject of resistance to penicillin was interesting. Some of the members present had seen cases which had failed to respond to quite large doses. He had heard of one case in which there was a double infection of syphilis and gonorrhoea ; in this case the syphilis appeared to be cured but the gonorrhoea persisted in spite of treatment with 2,400,000 units of penicillin.

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GUMMA OF THE THYROID GLAND

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Gumma of the thyroid gland is rare ; Stokes has seen the condition only twice. A number of individual cases, however, have been reported and the following one is typical.

Case report

A soldier aged 42 years reported sick with a swelling in the neck which he had noticed for the past year. He was transferred to my care on 22nd March 1945, as a routine Wassermann test had given a positive reaction ; the tentative diagnosis given was a branchial cyst. In addition to the painless swelling, he reported increasing difficulty over the past 12 months in swallowing solid or dry food, together with undue breathlessness on exertion.

History.—His father had tabes dorsalis. His mother had had 3 pregnancies ; the patient was the last child and was preceded by a sister who died in infancy. He had been married for 20 years and his wife's first child died " from pneumonia " at the age of 6 weeks. Two miscarriages followed. He denied having had venereal disease.

Examination.—Examination revealed a painless, non-tender, rather soft swelling underlying the left sternomastoid muscle in the anterior triangle of the neck. It was not pulsatile, moved slightly when he swallowed and did not appear to infiltrate the surrounding structures. The trachea was displaced to the right. The tumour was the size of a plum, and the glands in the posterior triangle of the left side of the neck were palpable, firm, non-tender and discrete. The patient was edentulous and showed anterior bowing of the tibiae ; no other stigma of congenital syphilis was noted. He was dull, apathetic and had some thinning of the outer parts of the eyebrows, but showed no other clinical evidence of myxoedema. No other abnormality was detected and there was no penile scar.

The blood Wassermann and Kahn tests were both strongly positive ; the cerebrospinal fluid was normal. Radiological examination showed the following : (1) some increased periosteal thickening of both tibiae and fibulae with a generally increased density of the left tibia ; (2) bronchitis and some dilatation of the aorta and displacement of the trachea to the right ; (3) a barium swallow showed no evidence of a diverticulum, the bolus passing without difficulty through the oesophagus, which was however pushed over to the right by the swelling.

Treatment.—A diagnosis of congenital syphilis was made and it was decided to undertake a therapeutic test to exclude gumma of the thyroid gland. Sodium iodide administration was commenced cautiously and later increased to a daily dosage of 90 grains. Bismuth oxychloride, 0·2 gramme, was given every 5 days and on the eleventh day of treatment small doses of mapharside were commenced. An excellent therapeutic response was obtained. On the eleventh day of treatment the thyroid swelling was decidedly diminished and the patient was mentally brighter. One month later only a small nodule could be felt in the left lobe of the thyroid, and 3 months after the institution of antisyphilitic treatment even this was no longer palpable. The general improvement, physical and mental, was marked and the eyebrows had returned to normal.

Literature of gumma of the thyroid gland

In congenital syphilis

In 1866 Lancereaux wrote : " We do not know of any case which gives evidence